a7

- appropriate buffer solutions for carrying out the immunological reaction between the primary antibody and the test sample, between the secondary antibody and the tau-primary antibody complex and/or between the secondary antibody and the marker;
- [possibly,] optionally, for standardisation purposes, a purified protein or a synthetic peptide containing one or more tau epitopes.

REMARKS

The specification has been amended to claim priority and add reference to an earlier filed PCT application as required under 37 C.F.R. § 1.78(a)(2). Further, the specification has been amended to reflect the section headings and organization format preferred by the United States Patent and Trademark Office. Support for the Summary of the Invention is found at page 5, line 31 bridging page 6, line 5. Also attached is an Abstract on a new page.

In this amendment, claims 12 and 13 are cancelled and claims 5-11, 15 and 16 are amended to modify the recitation of multiple dependency. The amendment to claim 9 finds support in the Specification at page 7, lines 5 and 6. The amendment to claim 15 finds support in cancelled claim12. Claims 1-11 and 14-17 are now pending. A clean set of the pending claims is attached hereto.

It is believed that no fee is due. Should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Deposit Account No. 01-2508/11362.0034.PCUS00.

CONCLUSION

In view of the foregoing amendments, applicants respectfully submit the claims are in proper form and condition for allowance. Applicants request that the claims be allowed and the application advanced to issue.

The Examiner is invited to contact the undersigned attorney at (713) 787-1438 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

Patricia A. Kammerer
Reg. No. 29,775
Attorney for Assignee
INNOGENETICS N.V.

HOWREY SIMON ARNOLD & WHITE, LLP
750 Bering Drive
Houston, Texas 77057-2198
(713) 787-1400

Date: March 5, 2001

PENDING CLAIMS FOLLOWING PRELIMINARY AMENDMENT

1. A method for the early detection and/or quantification of CNS damage in an individual, said CNS damage being caused by space-occupying lesions of the CNS, by invasion or metastasis of the CNS, by organisms, by anoxia or ischemia, by chemical agents, by physical agents or by a combination of these mechanisms, said method comprising the step of determining the level of tau in said individual and comparing it to the level of tau in control healthy individuals.

2. A method for the early in vitro detection and/or quantification of CNS damage in an individual, said CNS damage being caused by space-occupying lesions of the CNS, by invasion or metastasis of the CNS, by organisms, by anoxia or ischemia, by chemical agents, by physical agents or by a combination of these mechanisms, said method comprising the steps of:

   - obtaining a sample from said individual,
   - determining the level of tau in said sample and comparing it to the level of tau in control healthy individuals.

3. A method according to claim 2 in which the sample is taken from the cerebrospinal fluid of the individual.

4. A method according to claim 2 in which the sample is taken from the blood derivatives of the individual.

5. (Amended) A method according to claims 1 or 2 in which the space-occupying lesion of the CNS is a primary brain tumor, benign or malignant, brain metastasis, or a subdural haematoma.

6. (Amended) A method according to claims 1 or 2 in which the invasion or metastasis of the CNS is by leukemia, lymphoma or breast cancer.

7. (Amended) A method according to claims 1 or 2 in which the organisms are bacteria or viruses causing encephalitis or meningitis.

8. (Amended) A method according to claims 1 or 2 in which the anoxia or ischemia is caused by stroke, by cerebral infarction, by cerebral hemorrhage, by thrombosis, by perinatal asphyxia, by Binswanger disease or by vasculitis.

9. (Amended) A method according to claims 1 or 2 in which the chemical agent is gene therapy, pharmaceuticals, chemotherapy or exposure to chemical compounds.

10. (Amended) A method according to claims 1 or 2 in which the physical agent is a trauma, stroke, intracranial pressure or radiation.

11. (Amended) A method according to claims 1 or 2 in which CNS damage is detected and/or quantified in order to evaluate the effect of a certain treatment on said CNS damage.

14. A kit for the early diagnosis of CNS damage in an individual, said CNS damage being caused by space-occupying lesions of the CNS, by invasion of the CNS, by organisms, by anoxia or ischemia, by chemical agents, by physical agents, or by a combination of these mechanisms, comprising a tool for the detection of tau.

15. (Amended) A kit according to claim 16, wherein the marker is tau.

16. (Amended) A kit according to claim 14 characterised in that said kit comprises:

- a monoclonal antibody (primary antibody) which forms an immunological complex with an epitope of tau;
- a secondary antibody
  - which can be a monoclonal antibody recognising an epitope of the tau-primary antibody complex, but not recognising the primary antibody alone, or
  - which can be a polyclonal antibody recognising an epitope of the tau-primary antibody complex but not recognising the primary antibody alone, with said polyclonal antibody being preferably purified by immuno affinity chromatography using immobilized tau or immobilized tau-primary antibody complex;
- a marker either for specific tagging or coupling with said secondary antibody,
- appropriate buffer solutions for carrying out the immunological reaction between the primary antibody and the test sample, between the secondary

antibody and the tau-primary antibody complex and/or between the secondary antibody and the marker;

- optionally, for standardisation purposes, a purified protein or a synthetic peptide containing one or more tau epitopes.

17. A method to screen or monitor the effect of compounds which prevent or treat CNS damage comprising the step of determining the level of tau and comparing it to the level of tau in a control sample.